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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/518,414

08/30/2005

Johannes M. Van Den Brink

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01/28/2009

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EXAMINER

JOIKE, MICHELE K

ART UNIT

PAPER NUMBER

1636

MAIL DATE

DELIVERY MODE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Advisory Action</b> <b>Before the Filing of an Appeal Brief</b>	<b>Application No.</b> 10/518,414	<b>Applicant(s)</b> VAN DEN BRINK ET AL.	
	<b>Examiner</b> MICHELE K. JOIKE	<b>Art Unit</b> 1636	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 12 December 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on 9/15/08. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

#### AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
- (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ They raise the issue of new matter (see NOTE below);
- (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
- The status of the claim(s) is (or will be) as follows:
- Claim(s) allowed: 6,7,20 and 21.
- Claim(s) objected to: \_\_\_\_\_.
- Claim(s) rejected: 1-5,8-15,17-19,22,23.
- Claim(s) withdrawn from consideration: \_\_\_\_\_.

#### AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

#### REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see below.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_
13. ☐ Other: \_\_\_\_\_.

/NANCY VOGEL/  
 Primary Examiner, Art Unit 1636

Cont. of 11. Applicants argue that US 6,127,142 does not teach chymosin. Column 6, lines 43-48 merely indicates a target activity ratio for the deglycosylated *Rhizomucor miehei* aspartic protease.

US 6,127,142 teaches using a suitable milk clotting enzyme with an activity ratio similar or close to that of pure calf chymosin. They do not exclude chymosin; they do not teach using any aspartic protease except for chymosin. As explained in the prior office actions, chymosin is an implied choice to be used.

Applicants also request clarification for the statement that another advantage "would naturally flow from following the suggestion of the prior art." This statement was part of a paragraph in response to Applicant's argument that the present invention results from Applicants' desire to obtain the enzyme in higher yield. Nothing in the references would have provided the motivation necessary to arrive at the present invention. The point of the Examiner's statement was that the Examiner did not have to have the same motivation or "advantage" as the Applicants. The Examiner had another motivation or "advantage", as taught by the references, for combining them. The motivation is that Kasturi et al teach that N-linked glycosylation usually occurs at N-X-S/T sites, and N-glycosylation profoundly affects a protein's expression and function. (The entire obviousness rejection is cited in the first office action mailed September 18, 2007, and the reasoning behind it still stands.)

Applicants are also arguing that US 6,127,142 teaches a method for deglycosylating proteases for increased yield, and that the references do not teach using an NXT site on chymosin, unlike Applicants. If the Examiner is understanding the Applicants' arguments clearly, it appears that Applicants are arguing that US 6,127,142 teaches away. However, US 6,127,142 teaches the use of chymosin, and an NXT site present on a protease. While it does teach deglycosylating proteases, it does not teach complete deglycosylation. "The above treatment according to the invention results in removal of glycosyl moieties to an extent which depends on the degree of glycosylation and, when a deglycosylating enzyme is applied, the amount and the enzymatic activity of the enzyme and on the time of enzyme treatment. As an example, the coagulant produced natively by *Rhizomucor miehei* has three possible N-linked glycosylation sites i.e. sites having the sequence Asn-X-Thr/Ser at Asn.sup.79, Asn.sup.188 and Asn.sup.313, but it has been found that only two of these sites (79, 188) are glycosylated (Boel et al., 1986, Genetics, 1, 363-369). However, even if two possible glycosylation sites can be glycosylated by the homologous strain or a heterologous strain, the degree with which these sites are glycosylated may vary, e.g. according to the producing strain and the growth medium and conditions." col3., lines 34-48. "In accordance with the invention it is preferred that essentially all of the glycosyl moieties initially present in *Rhizomucor miehei* aspartic protease are removed, although it is expected that an enhancement of the milk clotting activity of such an enzyme will be found at lower degrees of glycosyl removal. Thus, the method according to the invention will preferably result in at least 10% deglycosylation, such as at least 20%. In more preferred embodiments, at least 50% of the glycosyl groups are removed such as least 75%." col. 3, lines 53-62. Furthermore, Kasturi et al teach that N-linked glycosylation usually occurs at N-X-S/T sites, and N-glycosylation profoundly affects a protein's expression and function, and US 5,800,849, col1, lines 25-27, teach an increase in cheese yield by glycosylating the protease, as noted by Applicants.

Lastly, the Applicants state that the Examiner's position was not understood for the 35 USC 103 rejection of claims 9-11 and 23. Applicants argued that the present invention results from Applicant's desire to obtain the enzyme in higher yield. First of all, nothing in the claims indicate that a higher yield is achieved or desired. Secondly, the Examiner has a different motivation or "purpose" for combining the references as noted in the September 18, 2007 office action. The fact that the Examiner does not have the same reason as the Applicants for creating the invention, does not make the Examiner's reasoning hindsight.